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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/551,188	04/17/2000	Axel Ullrich	7683-165	1301

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	25

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/551,188	ULLRICH ET AL.	
	Examin r	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the corresp ndence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on April 21, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/551,188 is acceptable and a CPA has been established. An action on the CPA follows.

Status of Claims

2. Claims 78-88 are pending in the instant application. Claims 17, 21, 25, 30 and 75-77 have been canceled and claims 78-88 have been added as requested by Applicant in Paper Number 24, filed April 21, 2003.

Claims 78-88 are currently under examination.

Change of Invention

3. Applicants have canceled pending claims directed to the originally elected invention, and have submitted new claims drawn to Invention III, originally claim 25, as detailed in the Election Requirement, Paper No. 14.

Specification

4. The disclosure is objected to because of the following informalities:

4.1 In the specification, page 11, line 3, the word "with" should be deleted to be grammatically correct.

4.2 On pages 47-48, section 6.2.4. refers to experiments in which MCK-10 is over-expressed, and phosphorylation and glycosylation is assayed. These experiments are referred to as Figure 4A and B, however, these experiments were actually demonstrated in Fig. 6A and B.

Appropriate correction is required.

Claim Objections

5. Claims 83 and 86 are objected to because of the following informalities: the first line of the claims recites a compound that "affects" MCK-10 activity, but parts (b) recites "modulates". Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 78-87 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Claims 78-87 are directed to methods of identifying antagonists or compounds that modulate the activity of or bind to the MCK-10 protein having the amino acid sequence of SEQ ID NO: 2 or a splice variant thereof, by contacting a test compound with the protein or cells expressing the protein, and determining whether the test compound binds to, inhibits binding of a ligand, or modulates the activity of the protein or results in a cellular change in a cell line. However, the methods do not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-

1099, Friday, January 5, 2001.

The instant specification discloses a nucleic acid identified as MCK-10 and various splice variants (MCK-10-1, MCK-10-2, MCK-10-3, MCK-10-4, Figure 2) encoding a protein that is identified as a receptor tyrosine kinase (SEQ ID NO: 2), originally isolated from a mammary carcinoma cDNA library, that is part of the transmembrane insulin receptor family. MCK-10 has an extracellular ligand-binding domain and an intracellular tyrosine kinase domain, and is believed to be involved in normal cellular responses. The specification discloses that MCK-10 nucleic acids are expressed in a number of normal tissue, epithelial cells, a wide variety of cancer cell lines and was expressed in all tumors tested. The specification also discloses an experiment on pages 47-48 in which MCK-10 DNA is over-expressed expressed in 293 cells, and the ability of the MCK-10 receptor to phosphorylate tyrosine in cellular protein is measured in the presence or absence of sodium-orthovanadate, which is a potent inhibitor of phosphotyrosine phosphatases. The results of the experiment (Figure 6) shows that a number of cellular proteins were phosphorylated, and there was an increase in phosphorylation of proteins in the presence of sodium-orthovanadate.

The specification asserts that identification of agonists and antagonists of MCK-10 receptor is desirable, because such compounds could be useful in treating diseases such as cancer. However, the specification has not established a substantial correlation between expression of the protein and cancer, so that a method of identifying potential agonists or antagonists of MCK-10 is not a specific and substantial utility. Although the gene may be expressed in many cancer cell lines and tumors, it is also expressed in normal cells or tissues. Additionally, even if the gene is expressed in many cancer cell lines and tumors, that does not

necessarily mean that the protein is also expressed. Haynes et al. (Electrophoresis 19 :1862-1871, 1998), studied 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript levels; for some genes, equivalent mRNA levels translated into protein abundances, which varied by more than 50-fold. Haynes concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (page 1863, 2nd paragraph, and Figure 1).

Determining if this protein is involved in cancer would require significant further research. The endogenous ligand(s) is not known, nor are the molecules in the phosporylation pathway that would be activated or inhibited by modulation of this receptor. There is no nexus between cancer and the molecules of the instant invention, so that these methods do not have a specific and substantial utility. A stated belief that a correlation exists between the protein of the instant invention and cancer, based on the limited information in the specification, is not sufficient guidance to use the protein in methods of identifying agonists or antagonists; identification of such compounds merely defines a starting point for further research and experimentation, and would not be considered useful by one of skill in the art.

The use of MCK-10 receptor requires further research to discover what the activities and biological significance of the protein is, if the receptor is involved directly or indirectly in any cancer, and whether either activation or inhibition of the receptor could be therapeutically advantageous for cancer treatment. It is possible that after further characterization, this protein might be found to be directly involved in abnormal cell proliferation, and that modulation of the receptor would be therapeutic. This further characterization, however, is part of the act of invention, and until it has been undertaken the Applicants' claimed invention is incomplete.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 75-87 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if the specification were enabling of how to use the polypeptide of SEQ ID NO: 2, the claims would not be enabled as written. For example, claims 78 and 85 encompass methods of identifying an antagonist of MCK-10 by determining if a test compound inhibits the binding of a ligand to the MCK-10. However, a test compound could bind to the MCK-10 protein and prevent binding of the ligand, but the test compound could also activate the receptor and therefor act as an agonist. Additionally, there is ligand identified for the MCK-10 protein. Claim 81 encompasses a method of identifying an antagonist of MCK-10 by determining if a test compound effects a cellular change in said cell line; however, a test compound could effect a cellular change by being an agonist.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 78-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 78-87 are indefinite because the independent claims (78, 81, 82, 83, 85 and 86) are incomplete method claims. The claims are not written with the different methods steps clearly recited. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved. For example, in claims 78 and 85, it is not stated how to determine whether the test compound inhibits binding of the ligand to the MCK-10 protein. In claim 81, it is not clear what cellular change occurs in the cell line. In claim 82, there is no step of isolating the peptide. In claims 83 and 86, there are no steps that describe how to determine if the MCK-10 activity is modulated.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B O'Hara

Patent Examiner